Dear Colleagues,

We are writing to let you know that 100,000 Genome Project cancer results are now available in the Genomics England cancer interpretation portal. All NHS GMCs will now receive their cancer results via the portal which replaces the web server which was a temporary platform for delivery of results. Results will no longer be issued in batches and will appear in the Portal as and when they are ready.

All results on the portal have been analysed using version 1.6 of the analytical pipeline (please see release notes below).

Portal users will be within NHS GMCs and each user will have personal credentials (Please note that N3 network is required). All NHS GMCs have now nominated Portal Leads and potential users should contact their Leads to gain access to results. Access to the portal can only be granted via these leads.

Release Notes for v1.6

1. ‘Tumour type’ and ‘Tumour subtype’ fields were renamed to ‘Disease type’ and ‘Disease subtype’ according to Genomics England cancer data model
2. ‘COSMIC content with low coverage’ is re-calculated with our in-house algorithm for coverage calculation (we used GATK in v1.4 and v1.5) and results can vary from the previous version by up to 10%
3. ‘Genome-wide coverage mean’ and ‘Unevenness of local genome coverage’ are re-calculated for autosomal chromosomes only in order to avoid variety due to the patient’s gender (v1.4 and v1.5 included calculation for all chromosomes) and results can vary from the previous version by up to 1%
4. Links to IGV viewer from the variants’ genomic coordinates are added. You will need to be connected to N3 network to be able to view it.
5. GnomeAD population germline frequencies are added to the variant grid
6. The list of actionable genes is updated (132 genes) according to the eligibility criteria for clinical trials at clinicaltrials.gov as of September 2017
7. The list of canonical transcripts was updated with Ensembl v90 transcripts
8. SV/CNV annotation have been corrected (see our previously circulated communication at https://public.huddle.com/a/WWZKkeM/index.html)
9. Mutation burden for non-synonymous SNVs in coding region has been re-calculated for cases issued in v1.4 (mutation burden in versions up to v1.4 was twofold overestimated due to an error in calculating total length of coding regions)
10. Mutational signature decomposition has been reviewed. In previous analytical pipeline versions the contribution of signature 1 was over-estimated. This was due to unnecessary normalisation of contextual frequencies of certain types of base substitutions. This step has been removed and has reduced the contribution of signature 1 and raised other signatures (e.g. signature 5). Following our communication with the team behind COSMIC signatures we are aware that the decomposition by non-negative least squares (our current method) tends to favor flatter signatures (i.e. signature 3) as well as over-fit and produce results with small contributions from multiple signatures in single genome analysis. Unfortunately, at the moment there are no published alternative methods but we expect new approach to be published and implemented in Q1 2018.
11. We refined the criteria for reporting loss-of-function germline variants. A variant is not reported if it’s ‘benign’ or ‘likely-benign’ with at least two stars in ClinVar database
12. Information on Sample Quality Control has been added to the Technical Information document